IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Rozhon *et al.*	Confirmation No.:	9130
Serial No.:	09/712,033	Art Unit:	1651
Filed:	November 14, 2000	Examiner:	Irene Marx
For:	ENTERIC FORMULATIONS OF PROANTHOCYANIDIN POLYMER ANTIDIARRHEAL COMPOSITIONS	Attorney Docket No.:	11133-004-999

DECLARATION OF THE INVENTORS UNDER 37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, Edward J. Rozhon, Atul S. Khandwala, Akram Sabouni, Gul P. Balwani, Jody Wai-Han Chan and David F. Sesin, citizens of the United States of America residing at 523 San Carlos Avenue, El Granada, California, 94018, 300 Winston Drive # 721, Cliffside Park, New Jersey 07010, 3398 Bing Hearst Drive, Suwanne, Georgia 30024, 6 Roberts Drive, Princeton, New Jersey 07010, 28065 Thorup Lane, Hayward, California 94542, and 557 Cambridge Drive, Benicia California 94510, respectively, do hereby declare and state that:

1. We are the inventors of the invention that is disclosed and claimed in the above-identified application, Serial No. 09/712,033 filed November 14, 2000, which claims priority to U.S. Application Serial No. 08/730,772 filed October 16, 1996, now abandoned. The claimed invention relates to methods for treating secretory diarrhea in animals by administering a pharmaceutical composition comprising an aqueous soluble proanthocyanidin polymer composition isolated from a Croton species or a Calophyllum species in which the

proanthocyanidin polymer composition is formulated to protect the proanthocyanidin polymer composition from the stomach environment, *e.g.*, coated with an enteric coating.

2. We are providing this Declaration to demonstrate that we conceived of and reduced to practice at least one embodiment of the claimed invention prior to August 16, 1996, which is the publication date of Davenport *et al.*, Pediatric Pulmonology, S13, Abstract 34.

3. Attached hereto as Exhibit 1 are copies of two pages from a Project Plan authored by co-inventor Edward J. Rozhon. We have reviewed Exhibit 1 and although the dates have been removed from this document, the date of this document is prior to August 16, 1996. Also, we confirm that the invention described in Exhibit 1 and all the acts relied upon in Exhibit 1 were carried out by one or more of us or at the direction of one or more of us in the United States of America prior to August 16, 1996. The pages set forth formulations of SP-303, which is an aqueous soluble proanthocyanidin polymer composition isolated from *Croton lechleri*, that protect SP-303 from acid, such as enteric coating and formulating with buffering or acid reducers.

4. Attached hereto as Exhibit 2 is a copy of Report No. SP-303-E-074 entitled "Effect of Enteric Coated SP-303 on Intestinal Fluid Accumulation in Cholera Toxin-treated Mice" ("the Report") authored by co-inventor Akram (Adam) Sabouni and Mei-Fong King, a laboratory technician acting under the direction of co-inventor Akram (Adam) Sabouni. We have reviewed Exhibit 2 and although the dates have been removed from this document, the date of this document is prior to August 16, 1996. Also, we confirm that the invention described in Exhibit 2 and all the acts relied upon in Exhibit 2 were carried out by one or more of us or at the direction of one or more of us in the United States of America prior to August 16, 1996. The Report summarizes the results of two experiments where enteric coated beads of SP-303 were orally administered to mice who had been given cholera toxin.

The experimental design is detailed on page 4 of 10 and page 5 of 10 of the Report. The mouse model used in the these experiments to measure the effect a test compound, in this instance enteric coated SP-303, has on fluid accumulation in mice given cholera toxin is a well known and art-accepted *in vivo* model of the effect of the test compound on diarrhea in animals.

5. On pages 5 of 10 to 8 of 10 the Report, results of the two experiments are presented and discussed. In Experiment I, group C, which was treated with enteric coated beads of SP-303, showed significantly reduced rations of fluid accumulation by an average of 32% and 29% as compared to control groups A and E, see Table 1 and Figure 1. In Experiment II, a single dose of enteric coated beads of SP-303 significantly reduced cholera toxin-induced fluid accumulation after a seven hour incubation with cholera toxin. Compared to control groups A and C, SP-303 enteric coated beads (group B) significantly reduced the ratios of fluid accumulation by an average of 45% and 38%, respectively, see Table 2 and Figure 2.

6. Attached hereto as Exhibit 3 are copies of notebook pages from laboratory notebook no. 333 of Mei-Fong King, a laboratory technician acting under the direction of co-inventor Akram (Adam) Sabouni. We have reviewed Exhibit 3 and although the dates have been removed from this document, the date of this document is prior to August 16, 1996. Also, we confirm that the invention described in Exhibit 3 and all the acts relied upon in Exhibit 3 were carried out by one or more of us or at the direction of one or more of us in the United States of America prior to August 16, 1996. The notebook pages set forth the raw data obtained from carrying out Experiment I discussed in the Report above.

7. Attached hereto as Exhibit 4 are copies of notebook pages from laboratory notebook no. 3368 of Mei-Fong King, a laboratory technician acting under the direction of co-inventor Akram (Adam) Sabouni. We have reviewed Exhibit 4 and although the dates

have been removed from this document, the date of this document is prior to August 16, 1996. Also, we confirm that the invention described in Exhibit 4 and all the acts relied upon in Exhibit 4 were carried out by one or more of us or at the direction of one or more of us in the United States of America prior to August 16, 1996. The notebook pages set forth the raw data obtained from carrying out Experiment II discussed in the Report above.

8. Exhibits 1 to 4 show that, prior to August 16, 1996, we had conceived and we, or persons acting under our direction, had reduced to practice the claimed methods by treating secretory diarrhea in an animal by orally administering a pharmaceutical composition comprising an enteric coated aqueous soluble proanthocyanidin polymer composition isolated from a Croton species or a Calophyllum species.

9. We declare further that all statements made in this Declaration of our own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date:_____ _____

Edward J. Rozhon

Date: August 11, 2006 Atul Khandwala

Atul S. Khandwala

Date:_____ _____

Akram Sabouni

Date:_____ _____

Gul P. Balwani

Date:_____ _____

Jody Wai-Han Chan

Date:_____ _____

David F. Sesin